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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,493	HANDFIELD ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 17-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 28-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/25/04 has been entered.

Status of claims

2. Claim 15 has been amended.

New claims 29-41 have been entered.

Claims 1-41 are pending in the application.

Claims 15, 16, 28-41 are under examination

Claims 1-14 and 17-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected group.

Claim Rejection - 35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying

4. Claims 15, 16 and 28- 41 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the revised guidelines on written description available at www.uspto.gov (O.G. published January

30, 2001). This is a written description rejection.

Claims 15, 16; 30, 31; 34, 35 and 38,39 are drawn to a method of detecting the presence of *A. actinomycetemcomitans* (Aa) or *A. actinomycetemcomitans* antigen (Aa antigen) in a test sample comprising contacting a test sample with an antibody or a fragment thereof that specifically binds to a purified immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52 (claims 15/16) or immunogenic polypeptide comprising SEQ.ID.NO: 52 (claims 30/31) or immunogenic polypeptide consisting essentially of SEQ.ID.NO: 52 (claims 34/35) or immunogenic polypeptide consisting essentially of at least 5 contiguous amino acids of SEQ ID NO;52 (claim 38 and 39), wherein the antibody or fragment thereof specifically binds *A. actinomycetemcomitans* or an *A. actinomycetemcomitans antigen* under conditions that allow formation of an immunocomplex between the antibody and the *A. actinomycetemcomitans* or the *A. actinomycetemcomitans* antigen; and detecting an immunocomplex, wherein detection of the immunocomplex indicates the presence *A. Actinomycetemcomitans* or A. *actinomycetemcomitans* antigen in the test sample.

Claims 28,29; 32,33; 36,37; and 40, 41 are drawn to a method of detecting the presence of *A. actinomycetemcomitans* antibody in a test sample comprising contacting a test sample with a purified immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52 (claims 28/29) or immunogenic polypeptide comprising SEQ.ID.NO: 52 (claims 32/33) or immunogenic polypeptide consisting essentially of SEQ.ID.NO: 52 (claims 36/37) or immunogenic polypeptide consisting essentially of at least 5 contiguous amino acids of SEQ ID NO;52 sample (claims 38/39) , wherein the polypeptide specifically binds to *A. actinomycetemcomitans* antibody under conditions that allow formation of an immunocomplex between the antibody and polypeptide SEQ.ID.NO: and detecting an

immunocomplex, wherein detection of the immunocomplex indicates the presence *A.actInomycetemcomitans* antibody in the test sample.

It is apparent that antibodies that bind to polypeptide consisting of the amino acid sequence, SEQ ID NO: 52 or to its claimed variants are required to practice the claimed invention (claims 15, 16; 30, 31; 34, 35 and 38, 39) that is drawn to detect the bacteria *A. actinomycetemcomitans* Aa (Aa antigen). Similarly, polypeptide, polypeptide variants are needed to practice the claimed invention (claims 28, 29; 32, 33; 36, 37; and 40, 41) that is drawn to detect the presence *A.actInomycetemcomitans* antibody in the test sample.

The specification teaches an isolated recombinant polypeptide comprising **the amino acid sequence**, SEQ ID NO: 52 and this full-length polypeptide SEQ ID NO: 52 consists of 179 amino acids and is useful in diagnosing *A. actInomycetemcomitans* antibody in a test sample. However, the claimed immunogenic polypeptide comprising SEQ.ID.NO: 52 or consisting essentially of SEQ.ID.NO: 52 read on an isolated polypeptide comprising (open language) SEQ.ID.NO: 52 plus unlimited and unknown amino acids and an isolated polypeptide consisting essentially of SEQ.ID.NO: 52 plus unlimited and unknown amino acids would result in an unknown polypeptides (considers as a variant) without any structure and other identifying characteristics such as function. Thus, said polypeptide variants are broader than SEQ.ID.NO: 52 and do not satisfy the written description guidelines. In addition, the specification does not teach an immunogenic polypeptide comprising at least 5 amino acids or immunogenic polypeptide consisting essentially of at least 5 amino acids or immunogenic polypeptide comprising or consisting essentially of SEQ.ID.NO: 52 and antibodies that bind to said immunogenic polypeptide (The examiner is considering them as variants/fragments). Therefore, said variants/fragments or antibodies that bind to said variants/fragments do not meet the guidelines on written description.

The specification fails to disclose any substitution, insertion or deletion or change in a polypeptide SEQ.ID.NO: 52 to obtain an immunogenic polypeptide comprising a fragment sequence of at least 5 amino acids or consisting essentially of at least 5 amino acids. The specification does not describe any use of said fragments as claimed in identifying *A.actinomycetemcomitans* infection (The examiner considers them variants/fragments). None of the above variants/fragments meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus variants as claimed are uncharacterized by this specification and are not asserted to belong to any known family of proteins *A. actinomycetemcomitans*. The specification fails to teach the structure or relevant identifying characteristics of polypeptide variants/fragments or antibodies that bind to said variants/fragments. Therefore, broadly claimed polypeptide variants/fragments sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Thus the specification fails to provide an enabling disclosure other than the method of detecting the presence of *A. actinomycetemcomitans* antibody in a test sample, using the polypeptide comprising the amino acid sequence SEQ.ID.NO: 52.

5. Claims 15, 16and 28- 41 are rejected under 35 U.S.C, first paragraph, because the specification while being enabling for a method of detecting the presence of *A. actinomycetemcomitans* antibody in a test sample comprising contacting a test sample with a purified immunogenic polypeptide comprising the amino acid sequence SEQ.ID.NO: 52 or immunogenic polypeptide consisting of the amino acid sequence SEQ.ID.NO: 52 wherein the polypeptide specifically binds to *A. actinomycetemcomitans* antibody in a test sample under conditions that allow formation of an immunocomplex between the antibody and the polypeptide SEQ.ID.NO: 52and detecting an immunocomplex, wherein detection of the immunocomplex indicates the presence *A.actInomycetemcomitans* antibody in the test sample does not reasonably provide enablement for

(a) method of detecting the presence of *A. actinomycetemcomitans* (Aa) or *A. actinomycetemcomitans* antigen in a test sample comprising contacting a test sample with an antibody or a fragment thereof that specifically binds to a purified immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52 (claims 15/16) or immunogenic polypeptide comprising SEQ.ID.NO: 52 (claims 30/31) or immunogenic polypeptide consisting essentially of SEQ.ID.NO: 52 (claims 34/35) or immunogenic polypeptide consisting essentially of at least 5 contiguous amino acids of SEQ ID NO;52 (claims 38/39), wherein the antibody or fragment thereof specifically binds *A. actinomycetemcomitans* or an *A. actinomycetemcomitans antigen* under conditions that allow formation of an immunocomplex between the antibody and the *A. actInomycetemcomitans* or the

A. actinomycetemcomitans antigen; and detecting an immunocomplex, wherein detection of the immunocomplex indicates the presence *A. actinomycetemcomitans* or *A.actInomycetemcomitans* antigen in the test sample and

(b) a method of detecting the presence of *A. actinomycetemcomitans* antibody in a test sample comprising contacting a test sample with a purified immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52 or immunogenic polypeptide consisting essentially of at least 5 contiguous amino acids of SEQ ID NO; 52 or polypeptide comprising SEQ.ID.NO: 52, wherein the polypeptide specifically binds to *A. actinomycetemcomitans* antibody under conditions that allow formation of an immunocomplex between the antibody and polypeptide SEQ.ID.NO: 52 and detecting an immunocomplex, wherein detection of the immunocomplex indicates the presence *A.actInomycetemcomitans* antibody in the test sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims have been discussed supra as above in Paragraph # 4.

With respect to SEQ.ID.NO: 52 variants/fragments:

The specification teaches an isolated recombinant polypeptide comprising **the amino acid sequence**, SEQ ID NO: 52 and this full-length polypeptide SEQ ID NO: 52 consists of 179 amino acids and is useful in diagnosing *A. actInomycetemcomitans* antibody in a test sample. However, the claimed immunogenic polypeptide comprising SEQ.ID.NO: 52 or consisting essentially of SEQ.ID.NO: 52 read on an isolated polypeptide comprising (open language) SEQ.ID.NO: 52 plus unlimited and unknown amino acids and an isolated polypeptide consisting essentially of SEQ.ID.NO: 52 plus unlimited and unknown amino acids that would result in an unknown polypeptide (considers as a variants) without any structure and other identifying

characteristics such as function. Thus, said variants are broader than SEQ.ID.NO: 52. In addition, the specification does not teach an immunogenic polypeptide comprising at least 5 amino acids or immunogenic polypeptide consisting essentially of at least 5 amino acids or immunogenic polypeptide comprising or consisting essentially of SEQ.ID.NO: 52 and antibodies that bind to said immunogenic polypeptide (The examiner is considering them as fragments). The specification lacks support for antibodies that specifically binds to antigen variants/fragments in a test sample. Further, it is not shown that these variants/fragments having no structural characteristics would bind to antibody present in the sample.

Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid sequences (i.e. fragments) for different aspects of biological activity cannot be predicted a priori and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and

functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide.

The specification provides no working examples demonstrating (i.e., guidance) enablement for variants/fragments and methods of detecting *A. actinomycetemcomitans* infection using said broadly claimed variants/fragments. The specification fails to provide an enabling disclosure for using variants of SEQ.ID.NO: 52 because it fails to provide guidance how a variant of SEQ.ID.NO: 52 is useful in diagnosing. infections. The specification provides no disclosure how a variant of SEQ.ID.NO: 52 may be used as a target for identifying infection because it fails to provide guidance whether this variant has the ability to bind to anti- *A. actinomycetemcomitans* antibodies. Therefore, the skilled artisan would not be able to use such broadly claimed variants. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as broadly claimed.

With respect to antibody variants/fragments:

It is apparent that antibodies that bind to polypeptide and its variants/ fragments are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. The specification fails to set forth variants/fragments of SEQ.ID.NO: 52 or antibodies that bind to variants/fragments of SEQ.ID.NO: 52. Therefore, methods using variants/fragments of SEQ.ID.NO: 52 are not disclosed. Antibody variants/fragments of SEQ.ID.NO: 52 read on

heavy, light chain and single chain antibody. None of these antibody fragments are amplified and sequenced.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the protein of heavy chain variable region and light chain variable region of variants/fragments which may contain less than the full complement of CDRs from the heavy and light chain variable regions of antibody in an unspecified order would retain the required binding function to *A.actinomycetemcomitans* antigen. The specification provides no direction or guidance regarding how to produce antibody that bind to variants/ fragments or antigen variants/fragments as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

The specification neither discloses nor teaches cDNA of variable regions (variable heavy chain and light chain variable) of the antibody that binds to *A.actinomycetemcomitans*. Further, the specification lacks support for LH construct HL construct. The specification does not teach

1. a heavy chain variable region that specifically binds to variant antigen
2. a light chain variable region binds specifically binds to variant antigen
3. a recombinant scFv antibody specific to Aa antigens of all serotypes, which comprises (a) a heavy chain variable region of an antibody specific to *A.actinomycetemcomitans* antigen variants/fragments of SEQ.ID.NO: 52 (b) a light chain variable region of an antibody specific to variants/fragments of SEQ.ID.NO: 52 comprising a linker between heavy chain region and the light chain variable region.

The present state of the art indicates that *A. actinomycetemcomitans* isolates were grouped in five biotypes II, VI, VIII, IX and X (see Malheiros et al Rev Saude Publica. 2004 Oct; 38(5): 723-728. Epub 2004 Oct 18) and suggests specific PCR techniques may be helpful in detecting putative periodontitis pathogens from subgingival sample and thus a single method could not be ideal, and using both traditional (culture) and molecular methods are recommended in the bacterial detection (see page 727). In addition, the specification fails to teach that a heavy chain and light chain by itself that specifically bind to variants/fragments of SEQ.ID.NO: 52. The specification fails to teach the structure or relevant identifying characteristics of an antibody fragments that specifically bind to variants/fragments of SEQ.ID.NO: 52 from all sero types of *A.actinomycetemcomitans*. Therefore, the methods that use variants/fragments of antibodies or variants /fragments of antigen do not satisfy the requirements under 35 U.S.C. 112, first paragraph for the reasons set forth as above. Therefore, the claimed antigen variants/ fragments of SEQ.ID.NO: 52 or antibody that binds to variants/ fragments of SEQ.ID.NO: 52 are yet to be identified in order to practice the broadly

claimed methods. The specification does not teach variants/ fragments of SEQ.ID.NO: 52 that are able to bind to antibodies from infected individuals. Thus, the specification is totally silent in teaching variants/ fragments of SEQ.ID.NO: 52 or antibodies that bind to variants/ fragments of SEQ.ID.NO: 52 so that one could detect the *A.actinomycetemcomitans* bacteria or A.actinomycetemcomitans bacterial antigens. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 28 and newly added claims 29, 32, 33, 36, 37, 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Flemmig et al 1996(Clinical and Diagnostic Laboratory Immunology; 3, 678-681) as set forth in the previous office action for claim 28.
Claims have been discussed supra as above in Paragraph # 4.

Flemmig et al disclose an immunoblotting method for detecting the presence of *A. actinomycetemcomitans* antibody (see abstract and page 679, left column under SDS-PAGE and immunoblotting). The method comprises contacting membrane proteins from *A. actinomycetemcomitans* that were separated by gel-electrophoresis (SDS-PAGE) with sera from infected individuals and thus read on contacting a test sample with a polypeptide of the claimed invention. After washing, the strips were incubated with goat anti-human IgA or IgG or

IgM conjugated with alkaline phosphatase. The presence of a band is considered positive because the antigen present on the strip bound to an antibody present in a test sample and forms an immunocomplex that is positively identified by goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The positive band indicates the presence of *A. actinomycetemcomitans* in a test sample (page 679, left column under SDS-PAGE and immunoblotting and figure 1). The disclosed outer membrane protein inherently contain claimed peptide variants/fragments of SEQ.ID.NO: 52 because the outer-membrane proteins were obtained from cell lysates that contain mixture of polypeptides including a peptide comprising at least 5 contiguous amino acids of SEQ.ID.NO: 52 and variants/fragments. Therefore, the prior art anticipates the claimed invention. In the absence of evidence to the contrary the disclosed prior art reads on the claimed invention since the OMP proteins bind to the specific anti-OMP antibodies. Characteristics such as including 5 contiguous amino acids of SEQ.ID.NO: 52 or variants/fragments of SEQ.ID.NO: 52 would be inherent in the preparations of OMP proteins. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed on 10/25 /04 have been fully considered but they are not deemed to be persuasive.

Applicant states that Flemmig does not teach SEQ.ID.NO: 52 mainly because the proteins disclosed are outer membrane proteins that are isolated from the in vitro culture and the presently claimed proteins are obtained by IVIAT methodology. Further applicant states that the examiner's inherency may not be established by probabilities and possibilities and cites several case laws of record.

It is the position of the examiner that the claim 28 is drawn to a method of detecting the presence of A.actinomycetemcomitans antibody in a test sample and is rejected correctly over a method of detecting the presence of A.actinomycetemcomitans antibody disclosed by Flemmig. Indeed the prior art method detected the presence of A.actinimycetemcomitans antibody by contacting outer membrane proteins from *A. actinomycetemcomitans* with a test sample. Applicant's attention is drawn to the language used in the claims "immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52". Further Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts and thus variants/fragments of SEQ.ID.NO: 52 read on outer membrane protein. Therefore, the disclosed method positively detects the presence of the antibodies and thus satisfies the purpose set forth in the preamble.

Applicant's argument that the protein used in the claimed method is obtained by IVIAT technology and therefore, the prior art method does not identify the antibody using outer membrane proteins in a sample is not right because applicant failed to show that the outer membrane proteins do not contain the claimed polypeptide variants/fragments of SEQ.ID.NO: 52. The examiner would like to bring applicants attention to the claimed method which requires the polypeptide comprising less than the amino acid sequence SEQ.ID.NO: 52 to detect an antibody. Further, antibodies produced during infection are expected to bind to outermembrane proteins of the bacteria since the relevant proteins are obtained during infection by "IVIAT" technology. Further, applicant is not claiming a method for detecting an antibody that specifically binds to the amino acid sequence SEQ.ID.NO: 52.

8. Claim 28 and newly added claims 29; 32, 33; 36, 37; and 40, 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Ebersole et al 1995(J.Dent Res 74 (2) 658-666) as set forth in the previous office action for claim 28.

Claims have been discussed supra as above in Paragraph # 4.

Ebersole et al disclose an immunoblotting method for detecting the presence of *A. actinomycetemcomitans* antibody (see abstract and page 659, right column under Western immunoblotting). The method comprises contacting outer membrane proteins from *A. actinomycetemcomitans* that were separated by gel-electrophoresis (figure1)) with sera from infected individuals and thus read on contacting a test sample with a polypeptide of the claimed invention. After washing the strips were incubated with goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The presence of a band is considered positive because the antigen present on the strip bound to antibody present in a test sample and forms an immunocomplex, which is positively identified by goat anti-human IgA or IgG or IgM conjugated with alkaline phosphatase. The positive band indicates the presence of *A. actinomycetemcomitans* in a test sample (page 660, left column under SDS-PAGE and immunoblotting and figure 2). The disclosed outer membrane proteins (OMP) contain the claimed peptide comprising at least SEQ.ID.NO: 52 because the outer-membrane proteins were obtained from cell lysates containing mixture of polypeptides including peptide comprising at least SEQ.ID.NO: 52. Therefore, the prior art anticipates the claimed invention. In the absence of evidence to the contrary the disclosed prior art reads on the claimed invention since the OMP proteins bind to the specific anti-OMP antibodies.

Applicants' arguments filed on 10/25/04 have been fully considered but they are not deemed to be persuasive.

Applicant states that the art of record does not teach SEQ.ID.NO: 52 mainly because the proteins disclosed are outer membrane proteins that are isolated from the in vitro culture and the presently claimed proteins are obtained by IVIAT methodology.

It is the position of the examiner that the claim 28 is drawn to a method of detecting the presence of *A.actinomycetemcomitans* antibody in a test sample and is rejected correctly over a method of detecting the presence of A.actinomycetemcomitans antibody disclosed by Ebersole et al. Indeed the prior art method detected the presence of A.actinimycetemcomitans antibody by contacting outer membrane proteins from *A. actinomycetemcomitans* with a test sample. Applicant's attention is drawn to the language used in the claims "immunogenic polypeptide comprising at least five contiguous amino acids of SEQ.ID.NO: 52". Further Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts and thus variants/fragments of SEQ.ID.NO: 52 read on outer membrane protein. Therefore, the disclosed method positively detects the presence of the antibodies and thus satisfies the purpose set forth in the preamble.

Applicant's argument that the protein used in the claimed method is obtained by IVIAT technology and therefore, the prior art method does not identify the antibody using outer membrane proteins in a sample is not right because applicant failed to show that the outer membrane proteins do not contain the claimed polypeptide variants/fragments of SEQ.ID.NO: 52. The examiner would like to bring applicants attention to the claimed method which requires the polypeptide comprising less than the amino acid sequence SEQ.ID.NO: 52 to detect an antibody. Further, antibodies produced during infection are expected to bind to outermembrane proteins of the bacteria since the relevant proteins are obtained during infection

by "IVIAT" technology. Further, applicant is not claiming a method for detecting an antibody that specifically binds to the amino acid sequence SEQ.ID.NO: 52.

9. Claims 15, 16 and newly added claims 30, 31,34,35, 38 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Snyder et al 1991 EPO0439210 or EPO 0439211 or EPO0439212 as set forth in the previous office action for claims 15 and 16.
Claims have been discussed supra as above in Paragraph # 4.

Snyder et al 1991 EPO0439210, disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or antigen extract with polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen (see page 2, lines 1-5, 51 through page 3, lines 1-15). They form an immunocomplex and said complex was detected with a label such as alkaline phosphatase or peroxidase etc (see example 1, page 9, line 51 through page 11, line 34), said Aa antigen is expressed during infection (se page 1, lines 57-64) causing periodontal disease and therefore the method detects the presence of Aa or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipated the claimed invention.

Or

Snyder et al, EPO 0439211 disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or extract of an antigen with polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen (see page 8, column 13 through column 14, line 8) and forms an immunocomplex and said complex is detected with a label such as alkaline phosphatase or peroxidase etc (see page 8 column 14, line 9 through page 9, column16, line 27), said Aa antigen is expressed during

infection (se page 1, lines 57-64) causing periodontal disease and therefore the method detects the presence of Aa (as low as 3000cells) or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipated the claimed invention.

Or

Snyder et al, EPO 0439212 disclose an ELISA method for detecting the presence of Aa or Aa antigen by contacting the sample suspected of containing a microorganism Aa or extract of an antigen with an polyclonal antibody conjugate, said antibody is specific to the Aa or Aa antigen and forms an immunocomplex and said complex is detected with a label such as alkaline phosphatase or peroxidase etc (see page 13, column 21 and page 14, column 23 through column 24, lines 31), said Aa antigen is expressed during infection (se page 1, left column lines 5 through right column) causing periodontal disease and therefore the method detects the presence of Aa or Aa antigen in a test sample. The disclosed polyclonal antibody specifically binds to Aa peptide comprising at least 5 amino acids of SEQ.ID.NO: 52 since the polyclonal antibodies are raised against all Aa polypeptides. The prior art anticipated the claimed invention.

10. Claims 15, 16 and newly added claims 30, 31, 34, 35, 38 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated Snyder et al 1992, EPO 537830 as set forth in the previous office action for claims 15 and 16.

Claims have been discussed supra as above in Paragraph # 4.

Snyder et al 1992, disclose an ELISA method for detecting the presence of Aa or Aa antigen from different patients suffering from periodontal disease by contacting the antigen extract in a surfactant mixture with an antibody, specific to *A. actinomycetemcomitans* (see

page 8, lines 17-45) in an ELISA plate. Immediately, peroxide/ antibody conjugate was added to the wells and sandwich complex formation was allowed for five minutes. After the last wash, the dye was added and the resulting signal was evaluated for the presence of Aa or Aa antigen in a test sample (see pages 8 - 9, lined 24-46 and Table 1, lines 5-15). The prior art anticipated the claimed invention.

Applicants' arguments filed on 10/25/04have been fully considered but they are not deemed to be persuasive.

Applicant states that Snyder et al do not teach or suggest the elements of the claimed invention because the antibodies used do not bind to a peptide comprising at least 5 amino acids of SEQ.ID.NO: 52. Applicant brings the examiner's attention to different parts of Snyder's polyclonal antibodies raised against bacteria and therefore, the antibodies are not specific to SEQ.ID.NO: 52. Further, applicant states that the claimed protein, SEQ.ID.NO: 52 is obtained by IVIAT technology.

The examiner disagrees with the applicant because the claimed method is drawn to detect the presence of *A.actinomycetemcomitans* antigen in a test sample not a method for detecting the presence of *A.actinomycetemcomitans* IVIAT antigen as set forth in the SEQ.ID.NO: 52. The polyclonal antibodies raised against bacteria would bind to the *A.actinomycetemcomitans* or *A.actinomycetemcomitans* antigen that is produced by the same bacteria *in vivo* and thus the method detects the presence of antigen in a sample

Remarks

11. No claims are allowed.

Conclusion

12. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives

transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number is 571-273-8300.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

14. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Respectfully,

Padma Baskar Ph.D